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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/960,234

Applicant(s)

JACOB ET AL.

Examiner

Cheyne D Ly

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 7-20, 22-24 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 21 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-26 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Applicants' arguments filed December 01, 2003 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. Applicant's clarification of the election of claims 1-6, 21, and 25 has been accepted.
3. The withdrawal of claims 7-20, 22-24, and 26 has been acknowledged.
4. Claims 1-6, 21, and 25 are examined on the merits.

### **CLAIM REJECTION UNDER - 35 USC § 102**

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-6 and 25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Eisen et al. (1998).
7. This rejection is maintained with respect to claims 1-6 and 25, as recited in the previous office action mailed May 30, 2003.
8. The instant rejection has been necessitated by Applicant's claim amendments.

### **RESPONSE TO ARGUMENTS**

9. Applicant argues that the claimed invention "is not drawn to relationships within gene expression profiles but is instead drawn to the examination of physiological traits." Applicant

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points to page 2 beginning at line 16 wherein the instant specification provides disclosure for the newly amended limitation of “physiological traits.” Further, Applicant argues that the claimed invention is directed to physiological correlations wherein there is a known relationship between physiological traits. Applicant’s arguments have been fully considered and found to be unpersuasive as discussed below. As to the critical limitation “physiological traits”, the limitation of “physiological” has been characterized by the Examiner, with the aid of the dictionary.com website, as “characteristic of the normal functioning of a living organism”; and the limitation of “traits” as “a genetically determined characteristic or condition.” Therefore, the disclosure of Eisen et al. for a method for determining the relationship between different genes of an organism via differential gene expression data has been reasonably interpreted as “physiological traits” as defined above.

10. Applicant argues that “Applicants first conduct a regression analysis to determine the relationship between the different physiological estimates. The results are then clustered. Eisen et al. simply cluster on the expression data—which is not physiological measurement.” Applicant’s argument directed to the difference between the “expression data” of Eisen et al. and “physiological measurement” of the claimed invention has been previously addressed above. It is noted the claim 1, step (b), recites “a correlation matrix using said correlation values.” Specific to the step of “a correlation matrix using said correlation values”, the method Eisen et al. comprises a step of using correlation coefficient for determining similarities between genes, and then, clustering analysis (page 14864, columns 1-2, Metrics § and Hierarchical Clustering §) as cited below.

11. Applicant argues that the color-coded graphical matrix of Eisen et al. “does not result in the showing of each element versus all the other elements.” It is noted that the limitation of “showing of each element versus all the other elements” is not present in claim 3. Therefore, Applicant’s argument has been considered to be moot.

12. Applicant argues that Eisen et al. “does not teach the use of color to ‘indicate a selected degree of correlation’ or use ‘cluster correlation matrix...to identify said relationships.’” In addition to Figure 2 as cited below, Eisen et al. discloses five separate clusters indicated by colored bars and by identical coloring of the corresponding region of the dendrogram. Each cluster denoted by a specific color corresponds to multiple genes functioning in (A) cholesterol biosynthesis...or (E) wound healing and tissue remodeling (Figure 1). The above citation discloses the limitation of ‘indicate a selected degree of correlation’ or use ‘cluster correlation matrix...to identify said relationships’ as argued by Applicant.

13. Applicant argues that “a human transcript is not a physiological determinant.” Applicant’s argument directed to the difference between the “expression data” of Eisen et al. and “physiological determinant” of the claimed invention has been previously addressed above.

#### **REJECTION RE-ITERATED**

14. Eisen et al. discloses a method for determining the relationship among physiological traits such as differential gene expression. The method of Eisen et al. comprises of using a hierarchical clustering algorithm based closely on the average-linkage method, which was developed for clustering correlation matrixes. For a set of  $n$  genes, an upper-diagonal similarity matrix is computed and node join two genes representing the most similar pair (§

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Hierarchical Clustering, page 14864, column 1, lines 1-4 to column 2, lines 1-6), as in claim 1, steps (a)-(d); claim 2; and claim 25.

15. Figure 2 discloses a color-coded graphical matrix representing the derived relationship of the physiological determinants, as in claim 3.

16. The source of the physiological determinants is 8,600 distinct human transcripts (§ Sources of Experimental Data, page 14864, column 1, lines 8-11), as in claims 4 and 6.

17. Claims 1 and 21 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Enright et al. (2000).

18. This rejection is maintained with respect to claims 1 and 21, as recited in the previous office action mailed May 30, 2003.

19. The instant rejection has been necessitated by Applicant's claim amendments.

#### **RESPONSE TO ARGUMENTS**

20. Applicant argues that Enright et al. does not disclose a computer program for analyzing physiological measurements. Applicant's argument directed to the difference between the protein data set of Enright et al. and "physiological traits" of the claimed invention is similar to the above argument of Eisen et al. directed to the expression data. The response above is being applied to Applicant's instant argument because protein data is consistent with the limitation "physiological traits" as defined above.

21. Applicant argues that Enright et al. does not provide a tool to create the correlation coefficients and then build the correlation matrix based on the cluster algorithm employed. It is noted the claim 1, step (b), recites "a correlation matrix using said correlation values."

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Enright et al. discloses in the initial steps sequence similarity search is undertaken to determine significant similarity relationships (correlation values) within a query database of size n proteins (page 452, column 2, Initial Steps §). “To facilitate clustering, the first step used was the symmetrification of the similarity matrix T” (page 453, Symmetrification of matrix §). “The processed matrix is recursively cluster by beginning a clustering operation for each row of the matrix” (page 454, Single linkage clustering §).

### **REJECTION RE-ITERATED**

22. Enright et al. discloses a method for using a computer program, GeneRace, written in ANSI C, and developed on a Sun Ultra workstation (§ System and method, page 452, column 2, lines 1-2), as in claim 21.

23. The method of Enright comprises using a recursive single-linkage clustering of the corrected matrix to allow efficient and accurate family representation for each protein in the dataset (Abstract etc.) and for multi-domain proteins two clusters of are artefactually linked (§ Multi-domain proteins, page 452, column 2, lines 4-31), as in claim 1, steps (a)-(d).

### **CONCLUSION**

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

25. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory

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period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. This application contains claims 7-20, 22-24, and 26 drawn to an invention nonelected with traverse, filed April 01, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

27. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

28. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and



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history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

29. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

31. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly  
6/23/04

*Ardin H. Marschel 7/4/04*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER